CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Bacillus Thuringiensis (Thuricide)

Chemical Code # 86, Tolerance # 01011
SB 950 # 215

September 18, 1998, revised March 21, 2007

I. DATA GAP STATUS[a]

Chronic toxicity, rat:	Data gap, inadequate study, no adverse effect indicated
Chronic toxicity, dog:	Data gap, no study submitted
Oncogenicity, rat:	Data gap, inadequate study, no adverse effect indicated
Oncogenicity, mouse:	Data gap, no study submitted
Reproduction, rat:	Data gap, no study submitted
Teratology, rat:	Data gap, no study submitted
Teratology, rabbit:	Data gap, no study submitted
Gene mutation:	Data gap, inadequate study, no adverse effect indicated
Chromosome effects:	Data gap, no study submitted
DNA damage:	Data gap, inadequate study, no adverse effect indicated
Neurotoxicity:	Not required at this time

[a] These studies are not required for microbial pesticides. See the Code of Federal Regulations 40, part 158.740, revised July 1, 2006. Therefore, they are not being required by DPR at this time. Acute toxicity studies for each formulation are required but are not listed in this document. Toxicology one-liners are attached.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
File name: T070321
Toxicology Summary prepared by J. Kishiyama and Gee, 9/18/98; Gee, 3/21/07.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

CHRONIC TOXICITY, RAT

116 026911 "Two-Year Dietary Administration in the Rat – Dipel," (Hazleton Laboratories America Inc., Project no. 375-123, 7/21/75). Dipel, assumed 100% pure, administered in the feed at concentrations of 0 (untreated) and 8.4 grams/kg to 60 albino rats/sex/group for 104 weeks. Body weight depressed for dipel treated group. UNACCEPTABLE, insufficient information: no individual body weight, organ weights and food intake; test article description, analyses of dosing material, no hematology, no urinalysis, no ophthalmology, limited histopathology. NOT UPGRADEABLE: insufficient number of dose levels. (J. Remsen (Gee), 7/15/85).

CHRONIC TOXICITY, DOG

No studies currently available.

ONCOGENICITY, RAT

116 026911, "Two-Year Dietary Administration in the Rat - Dipel", (Hazleton Laboratories America Inc., Project no. 375-123, 7/21/75). Dipel, assumed 100% pure, administered in the feed at concentrations of 0 (untreated) and 8.4 grams/kg to 60 albino rats/sex/group for 104 weeks. Body weight depressed for dipel treated group. No adverse effect indicated. Incidence of tumors in males and females in treated and control animals were comparable. UNACCEPTABLE, insufficient information: no individual body weight, organ weights and food intake; test article description, analyses of dosing material. NOT UPGRADEABLE: insufficient number of dose levels and not all animals included for full histopathology. Same study as listed under chronic toxicity for the rat. (J. Remsen (Gee), 7/15/85).

ONCOGENICITY, MOUSE

No studies currently available.

REPRODUCTION, RAT

No studies currently available.

TERATOLOGY, RAT

No studies currently available.

TERATOLOGY, RABBIT

No studies currently available.

GENE MUTATION

128 038039, " Mutagenicity Evaluation of Thuricide Technical Concentrate Lot XK-1080 in the Ames Salmonella/Microsome Plate Test", (D. R. Jagannath, Litton Bionetics, Inc., Project No. 20838, July 1978). Thuricide, technical, concentration (activity) not given, was tested at concentrations of 0 (DMSO), 0.5, 1.0, 10, 100, 500, or 1000 ug/plate with Salmonella typhimurium strains TA1535. TA1537, TA1538, TA100, and TA 98 without and with metabolic activation (Aroclor 1254 induced) for 48 hours. No evidence of a mutagenic effect. UNACCEPTABLE. Study lacks data on cytotoxicity, justification for doses and vehicle selection). This is probably an inappropriate assay for a microbial. (Gee, 7/15/85; Kishiyama and Gee, 9/18/98).

053 900276. Duplicate of 128 038039. Unacceptable study. (J. Gee, 7/15/85).

058 900276. Duplicate of 128 038039 and exact duplicate of 053 900276.

053 900275, "Mutagenicity Evaluation of Thuricide HPSC in the Salmonella/Microsome Plate Test", (D. R. Jagannath, Litton Bionetics, Inc., Lab Project No. 20838, August 1978). Thuricide HPSC, purity not given, tested at concentrations of 0 (DMSO), 0.5, 1.0, 10, 100, 500, or 1,000 ug/plate with Salmonella typhimurium strains TA1535, TA1537, 1538, TA100 and TA98 without and with metabolic activation (Aroclor 1254 induced) for 48 hours exposure. No adverse effect indicated. Testing this product via Ames Test is questionable. UNACCEPTABLE. Insufficient information on the effect of DMSO on Bacillus thuringiensis spores. Positive control (2-anthramine) with activation not effective. (J. Gee, 7/15/85; Gee, 9/21/98).

058 900275. Exact duplicate of 053 900275.

MUTAGENICITY PROTOCOLS & MISCELLANEOUS MUTAGENICITY

072 900274. Summary: "Mutation Possibilities of the Micro-organism (Bacillus turingiensis)", (Biochem Products - Solvay & Cie SA, Belgium). Bacillus thuringiensis is morphologically similar to the pathogenic agent Bac. anthracis. However, in the Steinhaus experiment (University of California), Bacillus thuringiensis did not undergo mutation involving a virulent power. No worksheets. (J. Gee, 7/15/85).

CHROMOSOME EFFECTS

No studies currently available.

DNA DAMAGE

128 038039, " Mutagenicity Evaluation of Thuricide Technical Concentrate Lot XK-10803-50 in the Ames Salmonella/Microsome Plate Test", (D. R. Jagannath, Litton Bionetics, LBI Project No. 20838, July 1978). Thuricide, technical, characteristics not given, tested at concentrations of 0 (DMSO), 0.5, 1.0, 10, 100, 500, or 1000 ug/plate with Saccharomyces cerevisiae strain D4 without and with metabolic activation (Aroclor 1254 induced) for 3-5 days. No evidence of a mutagenic effect. UNACCEPTABLE: study lacks data for survival frequency, and contamination; justification for dose and vehicle selection. NOT UPGRADEABLE: too few replicates. (Gee, 7/15/85; Kishiyama and Gee, 9/21/98).

053 900276. Duplicate of 128 038039. Unacceptable study. (J. Gee, 7/15/85).

058 900276. Duplicate of 128 038039 and exact duplicate of 053 900276.

053 900275, "Mutagenicity Evaluation of Thuricide HPSC in the Salmonella/Microsome Plate Test", (Litton Bionetics, Inc., Lab Project No. 20838, August 1978). Thuricide HPSC, purity not given, tested at concentrations of 0 (DMSO), 0.5, 1.0, 10.0, 100.0, 500.0, or 1,000.0 mg/plate with Saccharomyces cerevisiae strain D4 without and with metabolic activation for a 3-5 day exposure. Incubation temperature was 37°C and 30°C for activation and non-activation D4 yeast plates. No adverse effects. UNACCEPTABLE. Not upgradeable: no justification for strain (D4) selection and insufficient replicates/treatment. (Gee, 7/15/85).

058 900275. Exact duplicate of 053 900275.

NEUROTOXICITY

Not required at this time.

OTHER STUDIES

116 026912 A13-Week Dietary Administration - Rats; Dipel@ (W. A. Olson, Hazleton Laboratories, 3/16/73) Dipel, assumed to be 100%, no lot number, was fed in the diet at 0, 840 and 8400 mg/kg/day, with 10/sex/group. Hematology, clinical chemistry and urinalysis at initiation, week 4 and at week 13 on 5/sex/group. No ophthalmology. Limited histopathology. No toxic effects were reported. UNACCEPTABLE due to deficiencies in conduct. Not upgradeable. (D. McGee, 2/20/86; Gee, 9/22/98).

116 026910 AFour-week subacute inhalation toxicity study in guinea pigs; Dipel[7]@ (F. E. Reno, Hazleton Laboratories, 10/17/73) Ten albino guinea pigs per sex were exposed to nominal doses of Dipel at 0, 0.98 and 10.35 mg/l (gravimetric concentrations were 0.019 and 0.230 mg/l, attributed to the large particle size) for 6 hours/day, 5 days per week for 4 weeks. Sizing determinations showed that 85.96% and 92.36% were greater than 11 microns for the low and high dose groups. No hematology or blood chemistry data. Pathology was limited to the trachea, lungs, liver, spleen, skin and kidneys. Four males and four females in the high dose group had white spots in one or both eyes at termination. 11/20 low dose and 18/20 high

dose animals showed spots and/or areas of consolidation in the lungs. Possible adverse effect on eyes and respiratory system. UNACCEPTABLE. (D. McGee, 2/20/86; B. Davis, 11/5/86)

116 026918 AElimination rate of Bacillus thuringiensis spores administered to mice.@ (G. D. Hansen, Abbott Laboratories, Project no. 70111, 7/25/73) Male Swiss mice, 70/group, were given an IV injection of Dipel, lot-09-545-CD, of 0.1 ml of 10 mg/ml Dipel or 1.0 mg/ml in saline. The 10 mg/ml dose was equivalent to about 10^8 viable spores. At 1 and 2 weeks, blood was sampled and the organisms/ml determined. At 4, 10, 11 weeks and 5 and 5+ months, blood, liver, spleen and kidney were evaluated for viable Bacillus organisms. Spores were rapidly cleared from the blood with none present at 10 weeks. There were still some viable organisms in the spleen at the 5+ months sampling time. No vegetative cells were found apparently precluding an active infection. Deficiencies: No killed test organism control, no immunodepressed animals, one sex only, no dose quantification. (D. McGee, 2/20/86; B. Davis, 11/5/86)

140 060525 AThe effect of cyclophosphamide induced neutropenia on susceptibility of mice to lethal infection with Bacillus thuringiensis .@ (R. E. Bryant, J. A. Mazza, M. A. Green and L. R. Foster, Oregon Health Sciences University, 7/87) Male Swiss Webster mice were injected with cyclophosphamide to induce neutropenia. Control and neutropenic mice were dosed with B. Thuringiensis supsp Kurstaki or S. aureus by several routes: intravenous, intraperitoneal, subcutaneous, intranasal, wound injection and oral. Mice were divided into groups depending on WBC counts (<500, 500-999 and 1000 - 2000 WBC/mm^3) and exposed by either intravenous injection or oral in the diet. Cultures from blood and liver were made from mice that died. Mice were given a range of CFUs and survival reported. Survival, in general, was lower in neutropenic mice and decreased with increasing CFU doses. Survival following S. aureus injection was similar. No worksheet. Supplemental study. (Gee, 9/22/98)